Review of Intravenous Immunoglobulin in the Treatment of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

Saira B. Momin, DO
James Q. Del Rosso, DO, FAOCD

Abstract

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare and serious cutaneous adverse reactions. There is controversy over the use of intravenous immunoglobulin (IVIG) in the treatment of SJS or TEN. The lack of randomized controlled trials to assess the benefits and risks of IVIG is due to its low prevalence and the high mortality rate associated with these cutaneous adverse reactions, especially in TEN. This article reviews published literature on case series that either supports or refutes the use of IVIG in the treatment of SJS or TEN.

Introduction

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare, but serious and potentially life-threatening adverse cutaneous reactions commonly associated with the use of specific medications.[1–5] The main objective of this article is to discuss the use of intravenous immunoglobulin (IVIG) in the management of SJS and TEN and review evidence that either supports or refutes its efficacy for these two conditions.

What are the clinical manifestations of SJS/TEN?

TEN (or Lyell's syndrome) is manifested by the abrupt onset of fever; generalized dusky, erythematous rash; bullae; separation of large sheets of epidermis from the dermis; purulent conjunctivitis; mucositis of the mouth and genital area; and systemic toxicity.[1–3,6–9] The skin is painful to touch and any shearing force will cause the involved epidermis to slide off the dermis.[1–3,6,7] Usually, lesions manifest over a period of 2 to 15 days, but massive necrolysis involving the entire skin surface can occur in 24 hours. Anemia and lymphocytopenia are common and presence of neutropenia indicates a poor prognosis.[1–8] Inflammation of internal mucosal surfaces, such as the gastrointestinal and respiratory tracts, commonly occurs in TEN.[1,8,9] The condition can be associated with major metabolic abnormalities, multiorgan failure, sepsis, gastrointestinal hemorrhage, and pulmonary embolism. The overall mortality rate of TEN is approximately 30 percent.[1,4,8]

SJS and TEN have been reported to belong to a spectrum of reaction patterns, where SJS is at one end and TEN at the other.[1] The spectrum is divided into five categories: (1) bullous erythema multiforme (EM)—epidermal detachment involving less than 10 percent of body surface, with typical and atypical target lesions. EM is now considered a different disease than SJS/TEN; (2) SJS—epidermal detachment of less than 10 percent of body surface in association with widespread erythema or purpuric macules or flat atypical targets; (3) SJS/TEN overlap—epidermal detachment of 10 to 30 percent of body surface plus widespread purpuric macules or flat atypical targets; (4) TEN with spots—epidermal detachment of greater than 30 percent of body surface with widespread purpuric macules or flat atypical targets; and (5) TEN without spots—large sheets of epidermal detachment involving more than 10 percent of the body surface without purpuric macules or target lesions.[1,9] Figure 1 demonstrates confluent mucosal involvement of the upper and lower lips in a patient with SJS. Figure 2 shows genital lesions in the same patient with SJS.

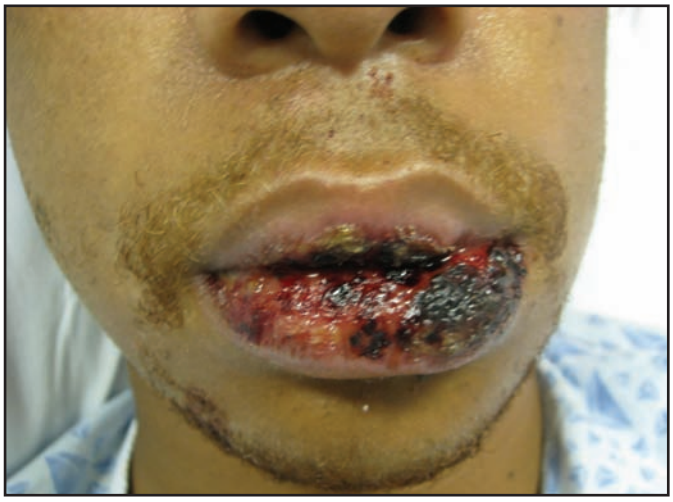

Figure 1. This figure demonstrates confluent mucosal involvement of the upper and lower lips in a patient with SJS.

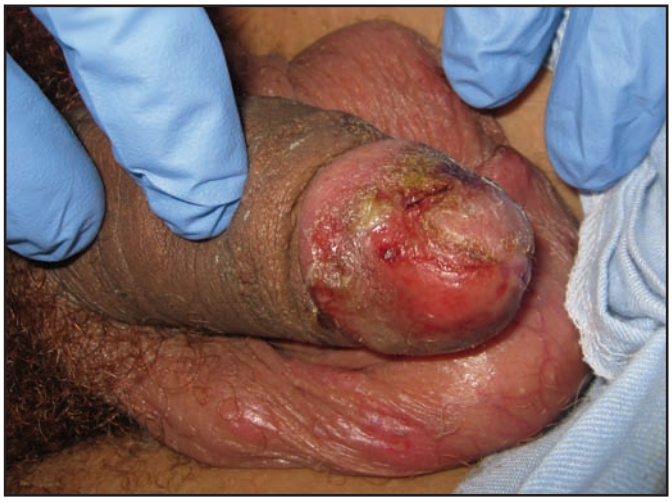

Figure 2. This figure shows genital lesions in the same patient with SJS.

What is the cause of SJS/TEN?

Drugs are the most commonly reported causative association with the development of SJS/TEN.[1,2,5,8] SJS occurs commonly in children and adolescents; whereas, TEN occurs in all ages.[1] The incidence of TEN and drug reactions generally is 2.7 times higher in the elderly than in a younger population, and mortality from TEN is twice as high in elderly patients as compared to younger patients.[1,2,7] The incidence of TEN and drug reactions generally is higher in HIV-infected patients, particularly in those with advanced disease.[1]

Many medications have been implicated in the cause of SJS/TEN, but the major offenders are sulfonamide antibiotics, particularly trimethoprim-sulfamethoxazole; aromatic anticonvulsants such as phenytoin, phenobarbital, and carbamazepine; beta-lactam antibiotics; nonsteroidal anti-inflammatory drugs; nevirapine; abacavir; lamotrigine; tetracyclines; and quinolones, especially ciprofloxacin.[1–5,8] In Asian populations, carbamazepine, phenytoin, and allopurinol are particularly common causes.[1] The period of greatest risk for developing SJS/TEN is in the first two months of treatment.[1]

How is the severity of illness evaluated in patients with TEN?

Several years ago, a scoring system for grading the severity of TEN, SCORTEN, was developed to assess the severity of illness and predict mortality associated with TEN.[1] SCORTEN should be calculated within the first 24 hours after admission and again on Day 3. The score is the sum of the following seven measured clinical variables: (1) age >40 years, (2) heart rate >120 beats per minute, (3) the presence of cancer or hematologic malignancy, (4) epidermal detachment involving body surface area >10 percent on Day 1, (5) blood urea nitrogen >28mg/dL (10 mmol/L), (6) glucose >252mg/dL (14 mmol/L), and (7) bicarbonate <20mEq/L. One point is given for each variable and the mortality increases sharply with each additional point. A SCORTEN score of 0 to 1 predicts 3.2-percent mortality, 2 predicts 12.1 percent, 3 predicts 35.3 percent, 4 predicts 58.3 percent, and a SCORTEN score of 5 or greater predicts 90.0-percent mortality.[1] SCORTEN has proven to be extremely accurate in predicting mortality.[1,3,7]

What is believed to be the immunopathogenesis of TEN?

TEN is considered a T-cell mediated disorder. In early stages of disease, there are mainly CD8+ lymphocytes in the blister fluid and epidermis and CD4+ lymphocytes in the dermis.[1,9] Monocytes are also present in the epidermis of TEN patients and in later stages of the disease, there is a relative decrease in lymphocytes and increase in monocytes.[1] Cytotoxic T-lymphocytes kill other cells by inducing apoptosis, which is an "immunologically silent" process that does not trigger an inflammatory response and occurs very rapidly.[1] A cascade of intracellular enzymes called caspases is activated when cytotoxic T-lymphocytes come in contact with target cells. The

caspase cascade is induced either through the perforin/granzyme or the Fas (CD95)-Fas ligand (FasL/CD95L) pathway.[1] Both Fas-FasL and perforin/granzyme are involved in triggering apoptosis in TEN.[1,2,6,8,9,11]

What is the treatment for SJS/TEN?

The primary treatment for SJS/TEN is discontinuation of the causative factor(s), usually an offending drug. The faster the causative drug is eliminated, the better the prognosis.[1,3,7] Another important element of treatment that has been suggested is supportive care in a burn unit or in intensive care.[1,7,11] There is some evidence that cyclosporine, cyclophosphamide, plasmapheresis, systemic corticosteroids, tumor necrosis factor-alpha (TNF-α) inhibitors, and IVIG may be beneficial; however, treatment with systemic corticosteroids and other immunosuppressive agents is controversial because of a possible increased risk of sepsis.[1,2,7,8,11]

What are the characteristics of IVIG?

The intravenous administration of exogenous pooled human immunoglobulin was originally licensed as antibody replacement therapy in patients with primary immunodeficiencies.[1,11] IVIG is derived from a plasma pool of several thousand donors and consists mainly of immunoglobulin G (IgG). A wide variety of antibodies, including autoantibodies against normal proteins such as Fas are found in IVIG.[1,6,11] The mechanism of action of IVIG is complex and not completely understood.[1,11] IVIG likely produces its therapeutic effects via a combination of many pathways, including interfering with the effector function of T cells, B cells, and monocytes, which involves blocking the interaction of Fas (CD95) with its natural ligand, FasL (CD95L).[1–4,6–9,11]

What adverse reactions are associated with use of IVIG?

The majority of IVIG adverse reactions are mild, with cephalgia noted as the most common. Other mild reactions include low-grade fever, flushing, chills, rhinitis, myalgias, wheezing, tachycardia, back pain, abdominal pain, nausea, and vomiting.[10,11] The occurrence of cephalgia is often correlated with elevated blood pressure, and therapeutic intervention prior to IVIG infusion may prevent this side effect.[11] A number of cutaneous eruptions secondary to IVIG infusion also have been reported with an urticarial eruption being the most common.[11] Slowing the infusion often resolves the mild adverse reactions, but urticarial reactions can become severe and generalized.[10,11] Also, IVIG may interfere with the efficacy of live vaccines and therefore administration of such vaccines should be deferred until six months after treatment is complete.[11]

Rare serious adverse effects have also been seen with IVIG infusion, including hypotension, cytopenia, serum sickness, disseminated intravascular coagulation, aseptic meningitis, alopecia, acute renal failure, acute tubular necrosis, proximal tubular nephropathy, osmotic nephrosis, stroke, myocardial infarction, deep venous thrombosis, anaphylaxis, SJS, hemolysis, seizure, syncope, acute respiratory distress, pulmonary edema, pulmonary embolism, acute bronchospasm, and transfusion-associated lung injury.[2] History of migraine headache predisposes patients to develop aseptic meningitis from IVIG treatment.[11]

Many patients who developed either acute renal failure or renal insufficiency associated with IVIG treatment had baseline renal insufficiency and/or risk factors for renal disease, but more importantly, approximately 90 percent of the patients who developed renal dysfunction received an IVIG product that contained sucrose as a stabilizer.[11] Sucrose is a disaccharide and cannot be enzymatically broken down when given intravenously, and therefore may cause renal dysfunction as a result of osmotic nephrosis.[11] Use of sucrose-depleted IVIG minimizes the risks of renal failure.[6] Dose reduction of IVIG is recommended in patients with renal insufficiency to limit the risk of proximal tubular dysfunction.[6] Also, use of IVIG is contraindicated in patients with immunoglobulin A (IgA) deficiency because of increased risks of anaphylaxis.[6]

What outcomes have been reported with the use of IVIG for treatment of SJS/TEN?

Randomized controlled studies have not been performed in the treatment of TEN because it is rare and associated with a high rate of mortality.[2,11] There are multiple, open-label, prospective studies, retrospective case series, and case reports in evidence of supporting IVIG in the treatment of SJS/TEN.

In a multicenter retrospective analysis of 48 consecutive TEN patients, Prins et al[2] correlated a positive outcome in patients treated with high-dose IVIG, especially when the treatment began earlier in the course of the disease.[2] IVIG treatment was initiated on average seven days after the onset of TEN and given over a period of 1 to 5 days at a mean total dose of 2.7g/kg

(range 0.65-5.8g/kg). Interruption of the progression of epidermal necrolysis was observed in 43 (90%) of the 48 patients within 1 to 6 days of treatment. All but one of the 43 patients who initially responded to IVIG achieved complete healing of skin and mucous membrane lesions within an average of 15 days, resulting in a survival rate of 88 percent at Day 45. Analysis of clinical and therapeutic parameters of the group of patients who survived after IVIG infusion and the group of patients who died revealed that IVIG infusion was shown to be initiated later in patients who died, the total dose of IVIG received by patients who died was lower than that received by patients who survived, and the coexistence of an underlying chronic disease (renal and/or cardiovascular insufficiency, ischemic and/or hypertensive disease, cancer, or infectious disease) was more frequent in the group of patients who died. This study also demonstrated that the potential of IVIG to inhibit Fas-mediated cell death is variable among IVIG batches and therefore may have been a possible cause of variability in the response of patients with TEN. It was concluded in this study that early treatment with IVIG at a total dose of 3g/kg over three consecutive days (1g/kg/day for 3 days) was safe, well tolerated, and effective in improving the survival of patients with TEN.[2]

Trent et al[3] conducted a retrospective analysis of 16 consecutive patients with TEN who were treated with IVIG using the SCORTEN system.[3] All 16 patients received IVIG treatment daily for four days. Of these 16 patients, 15 received 1g/kg/day and one received 0.4g/kg/day. The average time between the first cutaneous lesion and the start of IVIG treatment was 3.5 days. All of the patients showed clinical improvement and disease resolution. No further lesions developed subsequent to IVIG treatment after an average of 3.75 days, with total reepithelialization occurring in an average of 8.5 days. One death was believed to relate primarily to comorbidity associated with pre-existing medical conditions. The patient had been undergoing dialysis prior to contracting TEN and received a lower dose of IVIG. Despite the lower dose, the patient's lesions had resolved, but she experienced a fatal episode of asystole. Based on the SCORTEN system, 5.81 patients (36.3%) were expected to die. This study concluded that using predicted mortality as determined by the SCORTEN system, IVIG treatment significantly decreased mortality and was well tolerated.[3]

In an open, noncontrolled, pilot study by Viard et al,[4] 10 consecutive patients with TEN were treated in three clinical centers with IVIG at doses ranging from 0.2 to 0.75g/kg of body weight per day for four consecutive days.[4] Of these 10 patients, seven were treated with 0.75g/kg/day and the remaining three patients were treated with 0.2g/kg/day, 0.375g/kg/day, and 0.45g/kg/day. Time from onset to treatment ranged from 2 to 5 days. Time between onset of IVIG treatment and interruption of further epidermal detachment averaged 1.5 days and complete reepithelialization occurred on Days 4 to 12. In all 10 patients, the progression of skin disease was halted after IVIG infusion, which was accompanied by rapid skin healing and a favorable outcome without significant adverse effects.[4]

A retrospective study of 38 Korean patients with TEN during a 13-year period was conducted by Kim et al.[12] The involved body surface area ranged from 30 to 70 percent. Twenty-one patients received systemic corticosteroids and 14 patients received high-dose (1.6-2.0g/kg) IVIG treatment. Thirteen of the 14 patients survived. Based on SCORTEN, treatment with high-dose IVIG showed a trend to lower actual mortality (7.1%) than predicted mortality (16.8%). Adverse effects of IVIG including headache, myalgia, nausea, transient neutropenia, and Coombs positive hemolytic anemia, were observed in five patients. However, these conditions normalized after cessation of IVIG therapy.

Stella et al[7] reported their experience with treating TEN both with and without IVIG.[7] In their report, they treated eight TEN patients with extensive epidermal debridement and coverage with artificial skin substitutes in the pre-IVIG series (patients not treated with IVIG) and treated 23 patients with IVIG (0.7g/kg/day for 4 consecutive days) and conservative wound management in the IVIG series. The IVIG-treated group also received methylprednisolone at doses of 250mg every six hours for the first 48 hours of admission. Cessation of further epidermal detachment from the onset of IVIG therapy averaged five days and complete wound healing occurred after an average of 12.3 days. The average SCORTEN score was 3 in both groups with approximately 35 percent of patients expected to die. The observed mortality was 75 percent and 26 percent in the pre-IVIG and IVIG-treated groups, respectively. In four cases, the cause of death was septic shock and multiple organ failure. Other causes

of death were respiratory failure and disseminated intravascular coagulopathy.

Campione et al[13] described 10 patients suffering from TEN with a mean total body surface area (TBSA) of epidermal detachment of 44 percent who were treated with 0.4g/kg/day for five consecutive days (2g/kg total dose).[13] Time of disease onset and start of treatment averaged three days. The calculated SCORTEN at admission was 35 percent and the observed mortality after IVIG treatment was 10 percent. In nine patients, there was dramatic improvement just after one course of infusion at an early stage of the disease.

Lissia et al[8] demonstrated an observed mortality rate of 20 percent when the expected mortality based on SCORTEN was 66 percent in five severe TEN patients treated with IVIG and plasmapheresis.[8] In these patients, the therapeutic approach combined both IVIG and plasmapheresis. The treatment regimen was continuous infusion of IVIG 1g/kg/day for the first three days after admission and 0.5g/kg/day for the next three days, along with three total cycles of plasmapheresis on the second, fourth, and sixth day after admission. For each cycle, plasma (3000mL) was replaced with 70 percent pure albumin and 30 percent frozen human plasma. Cessation of epidermal desquamation was dramatic and rapid in all patients (mean 2.8 days), and 4 out of 5 patients completely healed (mean hospital stay 16.8 days). The one mortality was a patient who died of cardiopulmonary arrest. It was concluded in this report that use of IVIG and plasmapheresis for TEN has a rational basis and may be effective in improving survival outcome in severely affected patients.[8]

What outcomes have been reported with the use of IVIG for treatment of SJS/TEN in children?

In a retrospective study by Tan et al,[14] eight patients with TEN and four patients with SJS-TEN overlap treated with high-dose IVIG were analyzed.[14] The total administered dose of IVIG was 2g/kg body weight with the exception of two patients who received a total dose of 1.5g/kg body weight. The time separation between the first sign of cutaneous lesions, mucosal lesions, or epidermal detachment, and the initiation of IVIG administration, ranged from 3 to 22 days. The length of hospital stay ranged from 10 to 37 days. The survival rate was 91.6 percent, and of the 11 patients who survived the range of time to objective responsiveness was 2 to 8 days.

In a prospective, noncomparative, open study from Kuwait, Al-Mutairi et al[15] analyzed 12 consecutive patients with TEN admitted over a five-year period treated with a dose of 0.5 to 1.0g/kg/day of IVIG for 4 to 5 days.[15] Four of the 12 patients were children (age range 7–12 years). The average TBSA involvement was 57.5 percent. IVIG infusion was started 1 to 3 days after admission. The time required among these patients to arrest the progression of disease activity was determined to be 2.83 days. The duration of time needed for complete healing ranged from 5 to 13 days, with 12.5 days noted as the average duration of hospital stay. There were no deaths reported among the 12 treated patients. One patient developed pneumonia during the hospital stay, but no other systemic complications were encountered.

A retrospective series evaluated eight pediatric patients with TEN characterized as having widespread epidermal necrosis who were treated with IVIG (0.5-0.75g/kg/day for 4 consecutive days).[16] All eight children survived despite a mean body surface area involvement of 67 percent. The average length of time between onset of symptoms or signs of TEN to onset of treatment in the hospital was 3.2 days. The average time to arrest progression of disease was 2.1 days, with time to complete reepithelialization observed over an average of 8.1 days. Treatment-associated toxicity was not noted in any of the patients. The majority of complications were infectious, including gram-negative and gram-positive bacteremia and respiratory tract infections. One patient developed deep venous thrombosis requiring short-term anticoagulation with heparin.

In an open, uncontrolled study, Mangla et al[17] treated 10 TEN patients with IVIG 0.05-0.1g/kg/day for five consecutive days.[17] The average TBSA involvement was 66.7 percent and IVIG infusion was started on average within 3.2 days. A mean of 2.1 days to arrest progression of disease was observed, with an average of 8.3 days for complete reepithelialization. There were no mortalities reported. No systemic complications were encountered in these patients and no side effects from IVIG treatment were observed. This study demonstrated efficacy of low-dose IVIG in children with TEN.[17]

In a retrospective study, Metry et al[18] reported seven pediatric patients with SJS who were treated with IVIG, 0.3 to 1.0g/kg/day for four consecutive days, with the exception of one patient who received treatment on Days 1, 2, 4, and 5.[18] IVIG was initiated at an average of 2.7 days after onset of cutaneous blistering. Cessation of cutaneous

blistering was observed in all patients within an average of two days after IVIG was initiated. All of the patients survived and no IVIG-related complications occurred. Five of the seven patients had received systemic corticosteroids prior to or concomitantly with IVIG. The authors concluded that IVIG is a useful and safe therapy for pediatric patients with SJS or TEN after reviewing 28 published reports from pediatric literature and based on their experience with these seven cases.[18]

Similarly, in another retrospective study of 12 pediatric patients with SJS, treatment of IVIG in doses of 0.375 to 0.7g/kg/day for 3 to 5 consecutive days resulted in 100-percent survival.[19] Four of the patients initially received systemic corticosteroid therapy, but a switch to IVIG was made due to continued progression of disease despite corticosteroid treatment. IVIG treatment was initiated within an average of 4.25 days after the onset of SJS. Interruption of the progression of epidermal necrolysis was within a mean of 2.1 days in all 12 patients, and complete healing occurred within a mean of nine days. No severe adverse effects were recorded as a consequence of IVIG treatment.

Have any other case reports demonstrated that IVIG is effective in the treatment of SJS/TEN?

There has been numerous case reports demonstrating positive outcome from IVIG treatment in SJS and TEN.[20–25] Tan et al[25] reported good outcomes in two AIDS patients with TEN treated with IVIG at a dose of 1g/kg/day for two consecutive days.[25] In one case study, Hebert and Bogle[26] successfully prevented the development of SJS in a woman undergoing cardiac catheterization with history of four previous episodes of SJS after receiving intravenous contrast dye.[26]

Have any reports suggested that IVIG may not be effective for the treatment of SJS/TEN?

Most case series have demonstrated efficacy of IVIG in treating SJS/TEN. However, there have also been studies showing minimal or no benefit from IVIG treatment in SJS/TEN. Morici et al[27] evaluated 12 pediatric patients with SJS, seven of whom were treated with IVIG, two with systemic corticosteroids, and three with supportive care.[27] IVIG was administered in a single infusion at 1.5 to 2g/kg and was administered on an average of hospital Day 3. In the IVIG-treated group, the average duration of fever was eight days compared to 14 days in the non-IVIG group. The average hospital stay was 12 days for the patients treated with IVIG and 15 days for those in the non-IVIG group. No systemic complications were observed with IVIG therapy. Although duration of fever was shortened in patients treated with IVIG, statistical significance was marginal. The hospital stay was slightly shortened in patients treated with IVIG, but statistical significance was not reached. In this report, IVIG was determined by the authors to be of minimal value in treatment of SJS in children.[27]

Brown et al[28] performed a retrospective chart review that included 21 TEN patients not treated with IVIG and 24 TEN patients treated with IVIG 0.4g/kg daily for four days.[28] There was no statistically significant difference in age, sex, days from onset of symptoms to admission, presence of ocular or mucosal involvement, or history of systemic corticosteroid administration between those patients who received IVIG and those who did not. The average SCORTEN between the two groups was approximately equivalent—2.2 in the non-IVIG group versus 2.7 in the IVIG-treated group. Overall mortality was 28.6 percent (6 out of 21 patients) among patients in the non-IVIG group and 41.7 percent (10 out of 24 patients) among those in the IVIG group. Overall length of hospital stay and length of stay for survivors were longer in the IVIG group. Patients receiving IVIG had a higher number of complications per patient throughout the hospitalization than those not treated with IVIG. It was concluded in this report that there was no significant improvement in survival for TEN patients treated with IVIG at any level of severity.[28]

In a similar study, Shortt et al[29] looked at 32 patients with TEN.[29] There were 16 patients in the IVIG group receiving 0.5 to 0.9g/kg/day for 3 to 5 days and 16 patients in the control group. There were no significant differences between the groups with respect to length of hospital stay, incidence of sepsis, duration of mechanical ventilation, severity of systemic inflammation response syndrome, and multiple organ dysfunctions. IVIG was determined to decrease progression of the cutaneous lesions, but the time to healing did not differ between the two groups. The study concluded there was no significant difference in the mortality rate between the IVIG group and the control group (25% vs. 38%).[29] There were no complications or side effects noted in the IVIG-treated group.

In a prospective, noncomparative

study, each of 34 consecutive patients with SJS, SJS-TEN overlap, or TEN were treated with a total dose of 2g/kg of IVIG, except for three patients who each received a total dose of 1g/kg of IVIG.[30] In 27 cases, IVIG was infused over two days, and in seven cases, over 3 to 5 days. SCORTEN predicted 8.2 deaths (21%) while 11 (32%) actually occurred, which is higher than the 20-percent historic mortality rate for TEN in that institution. Most deaths were due to sepsis, pulmonary failure, and multiple organ failure. Epidermal detachment progressed in 22 patients, regressed in four patients, and did not change in seven patients. It was concluded that the results did not support the routine use of IVIG treatment for patients with SJS or TEN.[30]

A European observational study (EuroSCAR) reported experience with treating 281 patients with SJS, SJS-TEN overlap, and TEN.[31] In this trial, 87 patients were treated with supportive care only, 35 with IVIG only, 40 with IVIG plus systemic corticosteroids, and 119 patients with only systemic corticosteroids. The total dose of IVIG given ranged from 0.7 to 2.3g/kg over 1 to 7 days in both the IVIG only group and IVIG/corticosteroid group. The mortality rates were 25 percent (22 out of 87 patients), 34 percent (12 out of 35 patients), and 18 percent (7 out of 40) in the supportive care only group, IVIG only group, and IVIG/corticosteroid group, respectively. The study concluded no significant benefit from any treatment was observed.[31] Lastly, IVIG did not appear to reduce the severity of ocular complications of TEN in 10 IVIG-treated patients when compared with 18 historical controls.[32]

What can be concluded from available data on the use of IVIG for treatment of SJS/TEN?

Although each study has its potential bias, most case series have demonstrated the efficacy of IVIG in treating SJS or TEN. When compared to reports that have demonstrated efficacy of IVIG in treatment of SJS/TEN, reports showing minimal or no benefit of IVIG treatment may have had poorer outcomes due to the low dose of IVIG used and longer time from onset of disease to the use of IVIG. Many of the case series that observed positive outcomes with IVIG utilized a dosing regimen of 0.75 to 1g/kg/day for 3 to 4 consecutive days in the treatment of SJS or TEN. Fernandez and Kerdel[11] state when initiating IVIG treatment, a dose of 2g/kg per cycle is generally recommended, but a 3 to 4g/kg total dose is recommended in patients with TEN.[11] A cycle consists of the total dose divided into three equal doses, each given on three consecutive days with each infusion given slowly over 4 to 4.5 hours.[11] Despite the multiple reports available on the use of IVIG for the treatment of SJS/TEN, there is unfortunately a lack of randomized controlled trials to assess the benefits and risks and to standardize the optimal treatment protocol.

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Saira B. Momin, DO, is Dermatology Resident at Valley Hospital Medical Center, Touro University College of Osteopathic Medicine, Las Vegas, Nevada. James Q. Del Rosso, DO, FAOCD, is Dermatology Residency Director, Valley Hospital Medical Center, Las Vegas, Nevada, Touro University College of Osteopathic Medicine, Henderson, Nevada; Clinical Associate Professor, Dermatology, University of Nevada School of Medicine, Las Vegas, Nevada; Las Vegas Skin & Cancer Clinics, Las Vegas and Henderson, Nevada.

QUESTIONS • CHALLENGES • CONTROVERSIES